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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,177	01/23/2004	Mark Tengler	PHFB:1007	7865

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EXAMINER	
ANDERSON, JAMES D	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/764,177	TENGLER ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-21,24-43 and 45-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-21,24-43 and 45-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

CLAIMS 1, 5-21, 24-43 & 45-61 ARE PRESENTED FOR EXAMINATION

Applicants' amendment filed 4/9/2007 has been received and entered into the application. Accordingly, claims 1, 40 and 61 have been amended and claims 4, 22-23, 44 and 62-80 have been cancelled.

In view of the above amendments, the objection to claims 4, 23 and 44 is moot because the claims have been cancelled. The rejection of claim 61 under 35 U.S.C. § 112, 2nd Paragraph is hereby *withdrawn*. Also, the amendments and Applicants' remarks have overcome the rejections not reiterated herein from the previous office action. Such rejections are hereby withdrawn. The following rejections are either reiterated or newly applied and constitute the totality of issues remaining in the present application.

Response to Arguments

Applicants' arguments filed 4/9/2007 have been fully considered but they fail to persuade the Examiner of an error in his determination that the instant claims are *prima facie* obvious over Devane *et al.* in view of Dang *et al.* and Davis *et al.* Applicants argue that Devane *et al.* provide a composition that is delivered in a modified release; however the composition in operation delivers an active agent in a pulsed manner. Applicants thus assert that the composition of Devane *et al.* does not provide a second active agent for extended release. However, Applicants admit that the composition of Devane *et al.* provide a first active for immediate release and that the second portion of the active ingredient is released rapidly after an initial delay period (page 9 of Response). It is not clear to the Examiner how release after an initial delay period is not "extended release" as recited in the instant claims. Devane *et al.* explicitly disclose that the

second population of active ingredients contains particles coated with a "controlled release coating" (Abstract). Further, the modified release components of Devane *et al.* have release profiles that read on the release profiles recited in instant claims 7-8, 26-27 and 47-48 (see Table 3 of Devane et al.). Thus, it is apparent that "extended release" as recited in the instant claims is encompassed by and obvious over the modified release components as disclosed in Devane *et al.* With respect to Applicants' arguments that Devane *et al.* do not teach guaifenesin as the first active or phenylephrine as the second active, once a pharmaceutical composition is disclosed in the prior art it is well within the purview of the skilled artisan to substitute one drug for another in such compositions. Further, the secondary references applied in the present rejection provide ample motivation to combine guaifenesin and phenylephrine in a single composition. With respect to Applicants' argument that Devane *et al.* do not teach that the second active can include three or more layers of the second active agent, firstly it would impossible to know exactly how many layers of an active agent have been applied to a carrier. Using traditional spray-coating, there is no way to apply exactly "three of more layers". Secondly, the skilled artisan would be motivated to apply as much active agent as is necessary to achieve the desired therapeutic activity and/or release profile. With respect to Applicants' arguments regarding the Dang *et al.* reference, it is noted that the reference is only used as a motivation to combine guaifenesin and phenylephrine in a single composition, not as a teaching with respect to the claimed composition itself. Finally, in response to Applicants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The rejection of claims 1, 5-21, 24-43 and 45-61 as being obvious over Devane *et al.* in view of Dang *et al.* and Davis *et al.* is maintained for the reasons of record and reiterated below.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1, 5-21, 24-43 and 45-61 are again rejected under 35 U.S.C. § 103(a) as being unpatentable over Devane *et al.* (U.S. Patent No. 6,228,398; Issued May 8, 2001) in view of Dang *et al.* (U.S. Patent No. 6,462,094; Issued Oct. 8, 2002) (cited by applicants) and Davis *et al.* (US 2003/0049318 A1; Published Mar. 13, 2003) (prior art of record).[1]

The instant claims are drawn to enveloped pharmaceutical compositions comprising a first active for immediate release and a second active for extended release wherein the first and

[1] Devane *et al.* qualifies as prior art under 35 U.S.C. § 102(b). Dang *et al.* and Davis *et al.* qualify as prior art under 25 U.S.C. § 102(a) and 102(e).

second actives are disposed on separate carriers (*e.g.* Claim 1). Applicants state that the problem to be solved in the prior art at page 4, ¶ [0013]:

> "It has been found, however, that the present methods fail to provide an efficacious amount of a first active ingredient in an immediate release form and a second active that is provided as an extended release formulation that takes advantage of the pharmacological effect of the immediate release active to maximize the efficiency of the delivery and pharmacological action of the second active. Yet another problem is that certain drugs affect the release profile of a second drug that is being provided in a single dose. The present invention solves these problems in the art."

To solve the prior art problems as presented in the instant case, one skilled in the art would need the means to formulate an enveloped composition comprising a first active for immediate release and a second active for extended release (wherein the first and second actives are provided on separate carriers). The skilled artisan would also need a motivation to formulate such a composition with guaifenesin and phenylephrine. Examiner herein presents a *prima facie* case of why the instantly claimed compositions would have been obvious to one of ordinary skill in the art.

Devane *et al.* disclose multi-particulate modified release compositions that deliver active ingredients in a pulsed or bimodal manner (Abstract). One object of the invention is to provide a multi-particulate modified release composition in which a first portion of the active ingredient is released immediately upon administration and a second portion is released rapidly after an initial delay period (*i.e.* extended release) in a bimodal manner (col. 3, lines 51-56). The first and second components are disposed on separate carriers (*i.e.* particles) (col. 4, lines 10-14) and can be the same or different (col. 4, lines 14-16). The active ingredient-containing particles of the

second component are coated with a modified release coating (col. 4, lines 15-18). In a preferred embodiment, the first component is an immediate release component (col. 4, lines 24-26). The patentees further contemplate combined therapy. For example, when the first and second components are different, an enhancer compound or a sensitizer compound in another component of the composition may accompany the drug compound present in one component in order to modify the bioavailability or therapeutic effect of the drug compound (col. 6, line 64 to col. 7, line 8). **By modifying the excipients or coatings of the particles, the time-release characteristics of the active ingredient from each component may be varied** (col. 7, lines 38-42). The invention of Devane *et al.* is exemplified in a preferred embodiment as recited at col. 8, lines 22-29) (emphasis added):

> In a preferred embodiment, the multi-particulate modified release composition according to the present invention has an immediate release component and at least one modified release component, the immediate release component comprising a first population of active ingredient containing particles and the modified release components comprising second and subsequent populations of active ingredient containing particles.

The multi-particle modified release composition according to the reference may be incorporated into any suitable dosage form, including filling into capsules, such as hard or soft gelatin capsules or compressed into mini-tabs and subsequently filled into capsules (col. 10, lines 15-27), thus teaching an "enveloped" composition. The compositions taught in the reference can also include one or more inactives as instantly claimed (Table 2). The reference also discloses the instantly claimed dissolution rates recited in claims 5-8, 24-27, 40 and 46-48 (col. 12, lines 15-21 and Table 3).

Thus, while Devane *et al.* provide the means to formulate an enveloped composition of a first active for immediate release and a second active for extended release, they do not teach that the first active comprises guaifenesin or that the second active comprises phenylephrine. Devane *et al.* also do not teach that the second active is selected from the group consisting of a decongestant, an antihistamine, an expectorant, or an antitussive.

Dang *et al.* is provided as evidence that guaifenesin and phenylephrine compositions were known in the art at the time the present invention was made. The patentees disclose that guaifenesin has an expectorant action, which increases the output of respiratory tract fluid by reducing adhesiveness and surface tension (col. 2, lines 3-5). The compositions described in Dang *et al.*, comprising guaifenesin and phenylephrine, provide the immediate expectorant action of guaifenesin and the prolonged decongestant action of phenylephrine (col. 2, lines 11-13). The compositions may be prepared for oral administration in the form of powders, capsules, elixirs, syrups and the preferred forms of tablets or suspensions (col. 2, lines 15-17). The reference thus provides one skilled in the art with the motivation to formulate a composition comprising guaifenesin and phenylephrine wherein the patentees state that the combination produces a composition possessing "sympathomimetic decongestant and expectorant properties superior to the use of either one of the compounds alone" (col. 1, line 65 to col. 2, line 3).

Davis *et al.* disclose immediate and sustained release formulations of guaifenesin and additional drug ingredients, including antitussives (*e.g.* codeine) and decongestants (*e.g.* phenylephrine) (Abstract; page 4, ¶ [0045]). Said formulations relate to sustained release preparations in the form of capsules having beads or granules of both immediate release formulation and beads or granules of sustained release formulation (page 2, ¶ [0019]). The

reference thus teaches the limitations of claims 1, 9, 12-17 and 19-21, 28-30 and 32-39. Davis *et al.* explicitly contemplate capsules (*i.e.* enveloped composition) having a combination of "beads or granules of immediate release formulation and beads or granules of sustained release formulation" (*i.e.* disposed in separate carriers) (page 4, ¶ [0043]). They go on to state that the invention will be described in detail in the context of the bi-layer tablet embodiment (*id.*). "Granules" (page 4, ¶ [0043]) of immediate release guaifenesin read on guaifenesin "in a powder form" as instantly claimed *(e.g.* claim 10). The formulations of the invention can also include other excipients (page 4, ¶ [0050]), thus disclosing the limitations of claims 18 and 38. The reference thus discloses capsules containing both immediate release and sustained release formulations that can reasonably contain guaifenesin and phenylephrine.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

In the instant case, the prior art discloses compositions comprising guaifenesin and phenylephrine, both in immediate release and immediate/sustained release formulations. The prior art also provides methods for formulating drug compositions comprising immediate release beads and sustained released beads in an enveloped composition having the dissolution profiles instantly claimed. The prior art differs from the instant claims in that no single reference discloses enveloped compositions comprising an immediate release agent (*e.g.* guaifenesin) and

a sustained release agent that is a decongestant (*e.g.* phenylephrine), an antihistamine, an expectorant, or an antitussive disposed on separate carriers with the dissolution profiles instantly claimed. The level of ordinary skill in the art is that of an M.D., Ph.D. or pharmacist.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the multi-particle modified release compositions disclosed in Devane *et al.* by providing immediate release guaifenesin and extended release phenylephrine particles. Dang *et al.* and Davis *et al.* both provide the motivation to do so. Dang *et al.* disclose that combined guaifenesin/phenylephrine compositions provide immediate decongestant action of guaifenesin and extended expectorant action of phenylephrine. Davis *et al.* disclose compositions comprising immediate release guaifenesin and sustained release guaifenesin with additional drug ingredients, including the instantly claimed antitussives and decongestants (*e.g.* phenylephrine). Although Davis *et al.* exemplify bi-layer tablet formulations, capsules containing immediate release and sustained release beads are also disclosed. It is noted that the dissolution profiles disclosed in Davis *et al.* for sustained release formulations are longer than those instantly claimed. However, it well within the level of ordinary skill in the art to modify release profiles of drugs by changing the sustained release layer as evidenced by Devane *et al.* Thus, one skilled in the art had the means (Devane *et al.* and Davis *et al.*) and the motivation (Dang *et al.* and Davis *et al.*) to formulate an enveloped composition comprising an immediate release first active and a sustained release second active wherein the first and second actives are disposed on separate carriers and the first active is guaifenesin and the second active is phenylephrine. Applicants have provided no evidence of unexpected results with the instantly claimed compositions of guaifenesin and phenylephrine.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson
Patent Examiner
AU 1614

June 22, 2007

PHYLLIS SPIVACK
PRIMARY EXAMINER

6/22/07